# Sierra Leone Trial to Introduce a Vaccine against Ebola (STRIVE) Overview

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COMAHS

Sierra Leone Ministry of Health and Sanitation

CDC Centers for Disease Control and Prevention

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# Overarching Goal

- To accelerate introduction and use of an Ebola prevention vaccine among at-risk people in Sierra Leone with concurrent evaluation of the efficacy and safety of the vaccine


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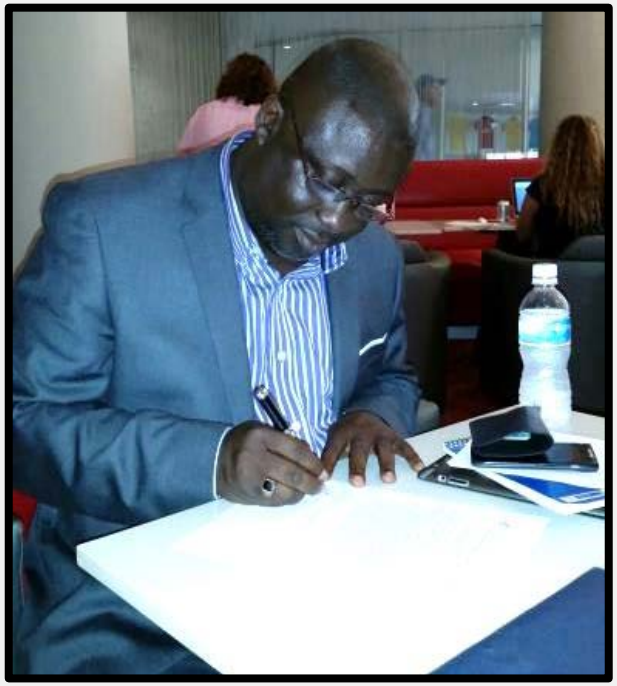
# Principal Partners

- **Sierra Leone**
  - College of Medicine and Allied Health Sciences (COMAHS)
  - Ministry of Health and Sanitation (MoHS)
- **United States**
  - Centers for Disease Control and Prevention (CDC)
  - Biomedical Advanced Research and Development Authority (BARDA)
- **Merck/NewLink**



Dr. Mohamed Samai, study PI and Acting Provost of COMAHS, signing a letter of agreement with CDC on December 17, 2014.

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# Contract Research Organization and Other Partners

- FHI360- training and site monitoring
- EMMES- data management/entry, safety reporting and statistical analysis
- Modality Solutions- cold chain expertise
- eHealth – in country implementation, supplies and staffing
- CDC Foundation - funding support


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# rVSVΔG-ZEBOV

- The vaccine used in STRIVE is the recombinant Vesicular Stomatitis Virus *Zaire ebolavirus* vaccine developed by Public Health Agency Canada / Newlink Genetics and now licensed by Merck

- The Vesicular Stomatitis Virus (VSV) envelope glycoprotein replaced with Ebola glycoprotein

- Live, replication-competent attenuated vaccine virus

- Single dose at $2x10^7$ pfu/mL intramuscularly (Diluted in saline from $1x10^8$ pfu/mL vial)

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# Study Objectives

- **Primary objectives**
  - Estimate the efficacy of the vaccine in preventing laboratory-confirmed Ebola virus disease (EVD)
  - Assess serious adverse events (SAEs) following administration of the vaccine

- **Secondary objectives**
  - Assess immunogenicity of rVSVΔG-ZEBOV at 2 x $10^7$ pfu/ml
  - Provide data on overall safety profile of rVSVΔG-ZEBOV

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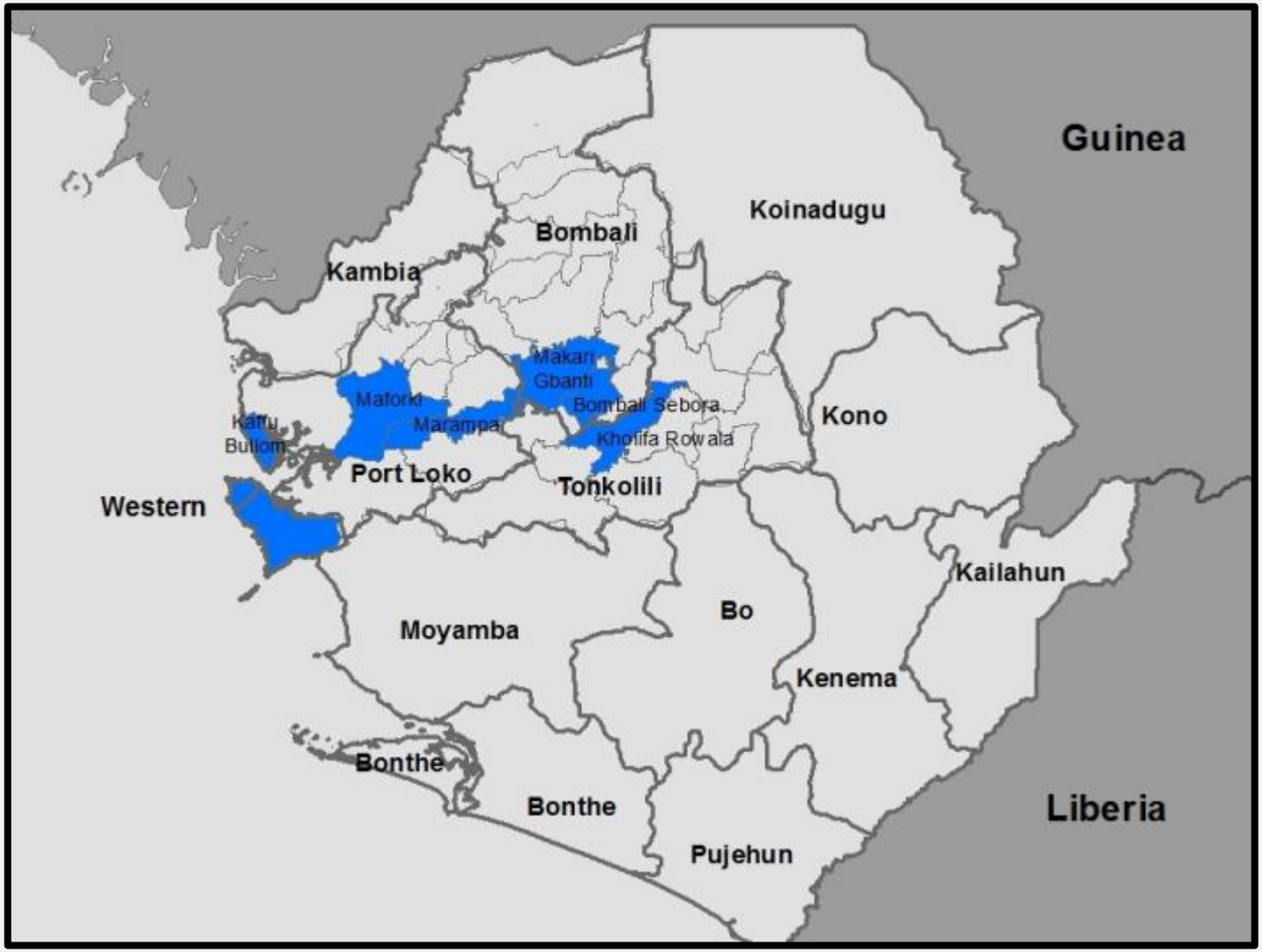
# Study Areas

**7 sites in**
**5 districts:**

Western Rural =1
Western Urban =1
Port Loko =3
Bombali =1
Tonkalili =1

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# Study Population

- **Health and other frontline workers in Sierra Leone**
  - All HCWs in both Ebola and non-Ebola- related healthcare facilities
  - Surveillance teams, ambulance teams, burial workers, and swabbers of the deceased
  - Pharmacy, cleaning, lab, security, and administrative staff at health facilities
  - Both nationals and expatriates are eligible if they anticipate living in Sierra Leone for the next 6 months
  - Approximately 6000 HCW needed

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# Study Design

- **Unblinded, randomized trial of vaccine with no placebo**
  - Enrolled participants will be randomly assigned to take the vaccine at enrollment or about 6 months later
  - Participants will be monitored for symptoms of Ebola Disease and to identify if they have any severe adverse events

- **Vaccine efficacy measured by comparing EVD incidence density rate in persons vaccinated after enrollment versus those not yet vaccinated (deferred vaccination group)**

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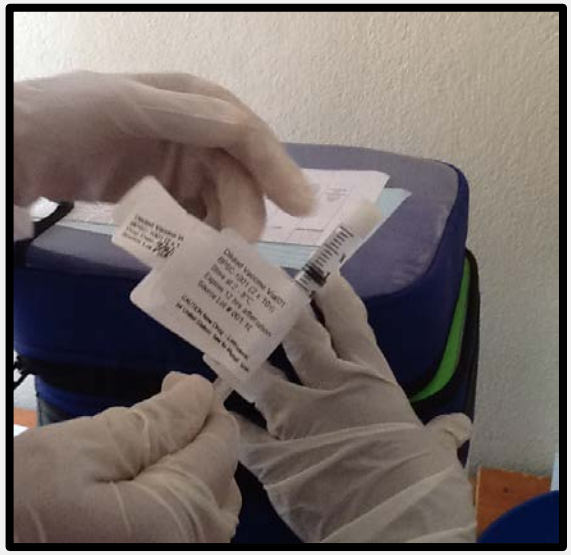
# Enrollment and Vaccination Steps

- **Screening and eligibility confirmation**
- **Consent for pregnancy testing (for women aged 18-49 years)**
- **Urine pregnancy test**
- **Consent for study enrollment**
- **Randomization**
  - to immediate or vaccination in 6 months
- **Vaccination**
  - (either immediate or in 6 months)
- **Observation for 1 hour following vaccination**



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# Follow-up of Study Participants

- **Participants will be monitored for severe adverse events for 6 months following vaccination**
  - Participants are given a cell phone to call study staff in case of fever or a new or worsening medical condition
  - Call center number provided
  - Participants are contacted monthly to assess their health

- **Free medical care is provided through a network of study providers for care of acute illnesses for the duration of the participant's involvement in the trial**

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# Evaluation of Possible Ebola in Study Participants

- **Several approaches for identification of suspected Ebola among study participants:**
  - Self-report of symptoms by participants to study staff via call center
  - Liaison with clinical partner so there is immediate notification of possible Ebola in a study participant at Ebola Holding Center
- **In addition to sample collected for clinical/diagnostic purposes, a second sample collected at presentation of patients meeting case definition for testing by study laboratory and study procedures.**

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# Vaccine Safety Sub-Study

- **FDA requirement to conduct safety sub-study at the start of the trial**
- **>400 enrolled at one study site in Western Rural area:**
  - >200 participants vaccinated immediately
  - >200 vaccinated later
- **Participants evaluated on day 0 prior to leaving the enrollment and vaccination site and days 1, 3, 7, 14 and 28**
- **Participants complete a daily diary card for days 1-28**
- **Study nurse calls them to assess symptoms**
  - will review information collected on the diary card as needed

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# DSMB and Safety Reporting

- **DSMB of five members representing:**
  1) Public health ethics;
  2) Biostatistics;
  3) Clinical trial safety monitoring experience;
  4) Adult clinical care in West Africa;
  5) Sierra Leone public health concerns.
- **Review weekly data during sub-study**
- **Monthly meeting of DSMB for overall safety data**
- **SAEs (related and unrelated) reported according to stipulations of FDA and Pharmacy Board Sierra Leone**

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# Immunogenicity Sub-Study

- **Plans to collect serum from 200 – 1000 vaccinated participants**
  - Day 0 (baseline)
  - Day 28
  - Month 6
  - Month 12
- **Planning to conduct at vaccination site in large hospital in Western Urban (Freetown)**
- **Serum separated in Sierra Leone and stored at -80 C**
- **Merck will contract Focus Diagnostics to conduct validated assays**
  - Anti-GP IgG antibodies by ELISA
  - Plaque Neutralization assay

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# Sample Size and Analysis of Overall Trial

- **Event driven sample size:**
  - For VE of 50%, power of 80% and Type 1 error of 0.05: need 67 events
  - Initial epidemiology suggested needed approximately 6000 HCW

- **Interim analyses**
  - At accrual of 17, 33, 50 events and final analysis at 67 events.
  - No stop for futility (incidence density ratio = 1)
  - Stopping rules for IDR >0.5 (evidence of protection) or if IDR >2 (evidence of harm)

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# Safety Pausing Rules

- One or more SAE(s) judged related to vaccination occurs (including a sudden unexpected serious adverse reaction (SUSAR)) OR
- Anaphylaxis or bronchospasm within 4 hours of injection, indicative of an immediate hypersensitivity reaction to the study injection OR
- 15% of participants experience a grade 3 (safety-substudy) or higher event judged related to study vaccine, excluding local injection site reactions that decrease to < grade 3 within 24 hours OR
- An AE pattern of concern occurred.

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# Results to Date

- **Over 1850 enrolled and over 850 vaccinated (May 3 2015)**
- **Safety profile to date consistent with other trials**
- **No SAEs related to vaccine**
- **Safety sub-study completed enrollment**
  - >400 enrolled
  - Calls continue for another 1-2 weeks
  - No unexpected safety signals to date
- **No study participant to date with possible Ebola**
  - Medical algorithm to differentiate side effects from EVD is working

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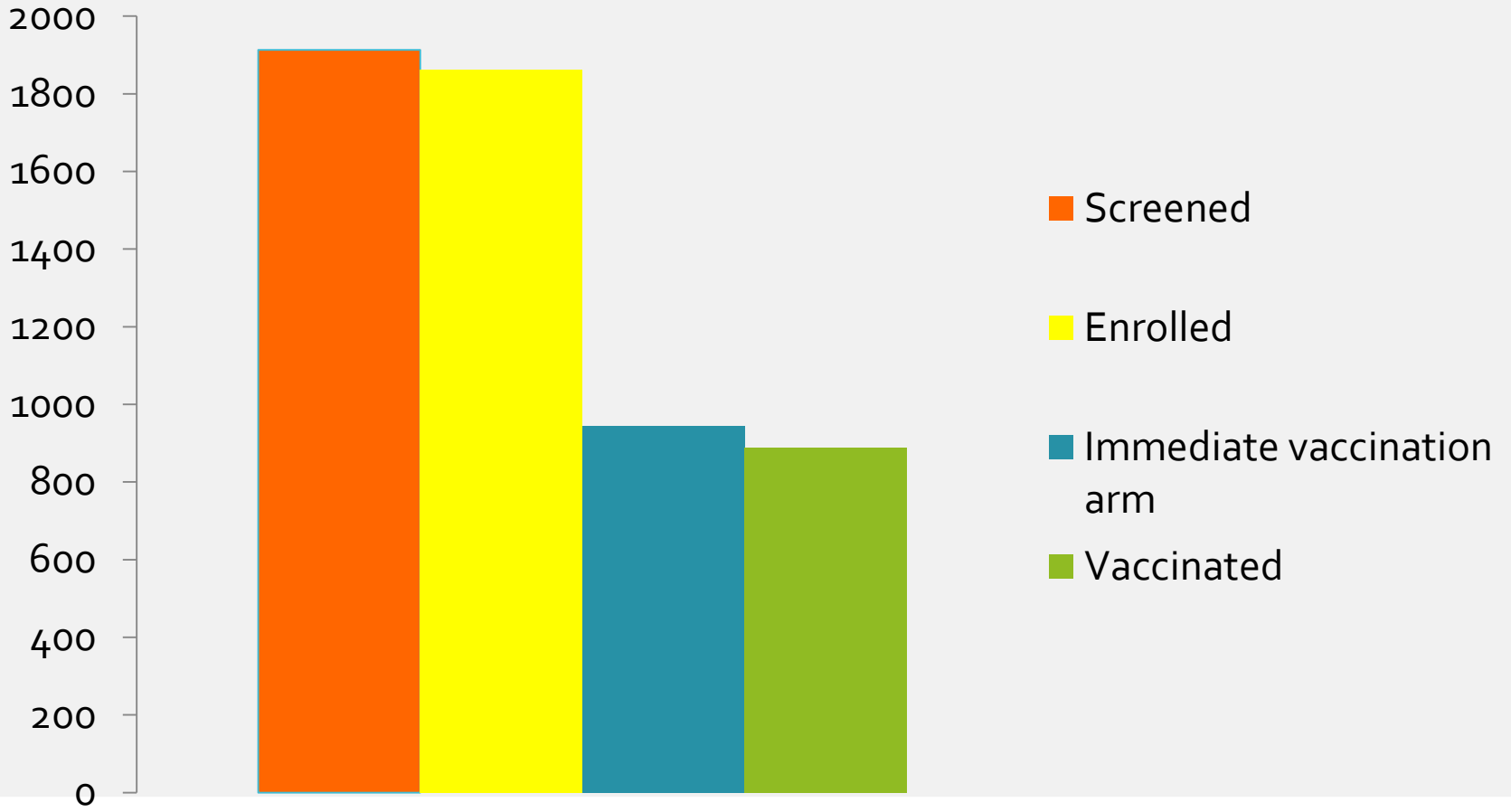
# Cumulative enrollment and vaccination, 4 sites, April 9-May 3, 2015

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Last updated May 3 2015

# Study Roll Out and Timeline

- **Seven sites launched:**
  - April 9th (study launch) to May 11th
- **Enrollment to continue until approximately June 2015**
- **Deferred group will be vaccinated October- December 21, 2015**
- **Study ends in approximately June 2016**


Renovating the COMAHS Conference Center, January 29 –March 5, 2015


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## Standard EVD case definition:

**Temperature ≥ 38.0° C AND three or more of the following symptoms:**

- Headache
- Loss of appetite
- Fatigue
- Muscle/joint pain
- Diarrhea
- Unusual bleeding
- Difficulty breathing
- Nausea/vomiting
- Abdominal pain
- Difficulty swallowing
- Hiccups

## Modified EVD case definition for STRIVE participants in immediate post- vaccination period:

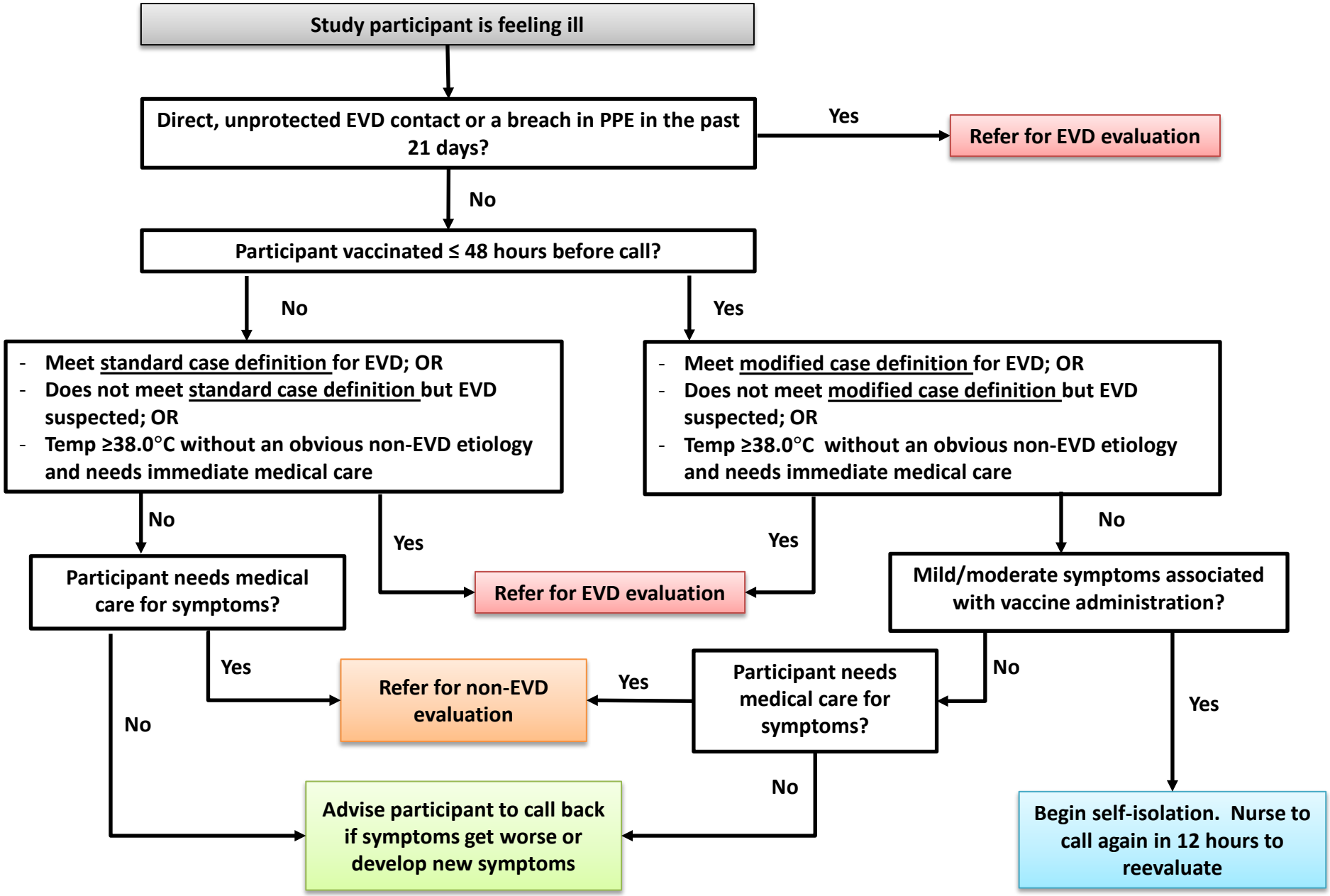
**Temperature ≥ 38.0° C AND three or more of the following symptoms:**

- Headache
- Loss of appetite
- Fatigue
- Nausea
- Muscle/joint pain
- **Diarrhea**
- **Unusual bleeding**
- **Difficulty breathing**
- **Vomiting**
- **Abdominal pain**
- **Difficulty swallowing**
- **Hiccups**

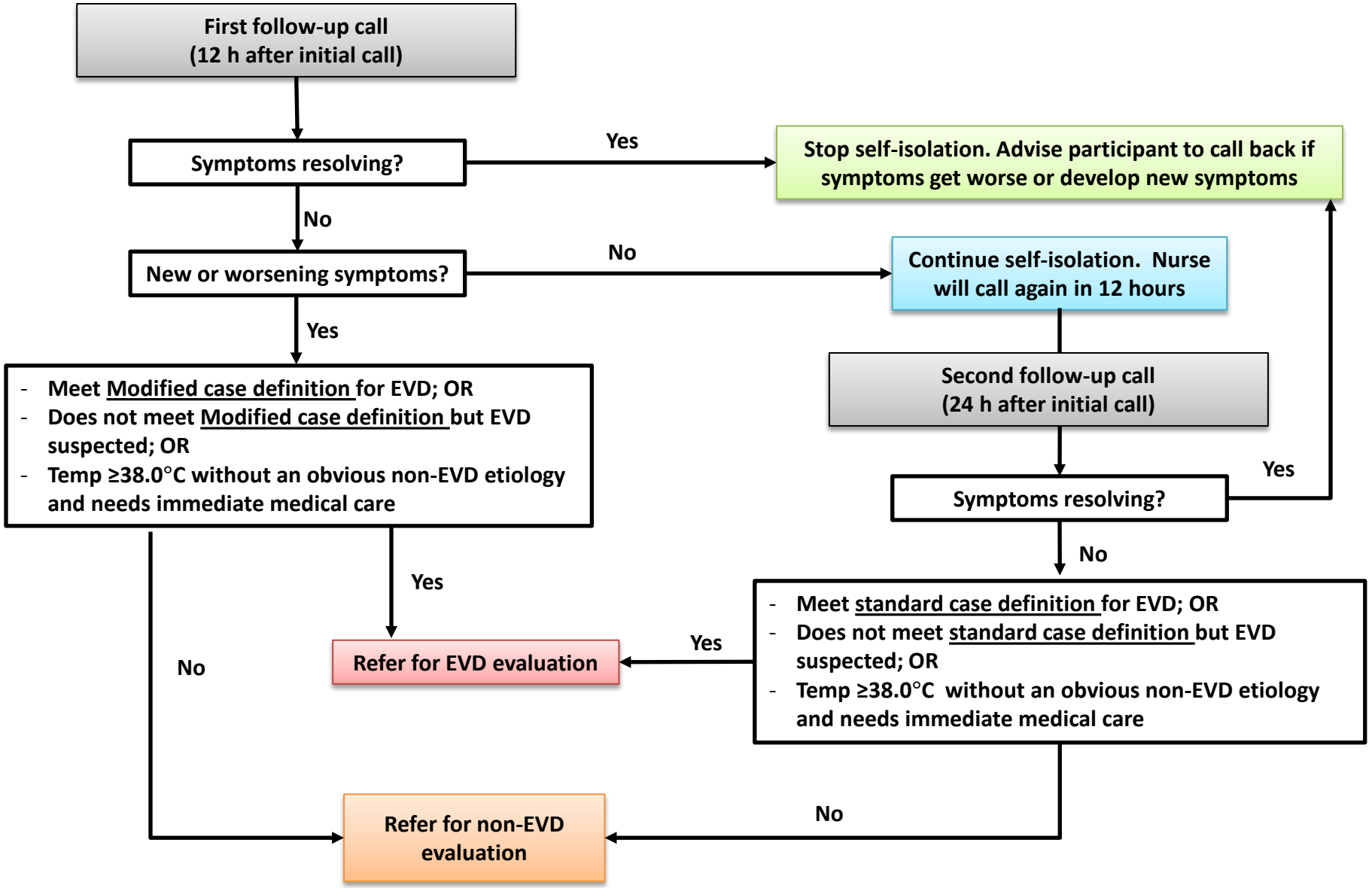
**To meet the modified case definition, the reported symptoms must include at least 1 of the symptoms* in the highlighted box**

*not known to be related to the study vaccine

# Medical Condition Assessment Algorithm



# Follow-up for Post-Vaccination Reaction

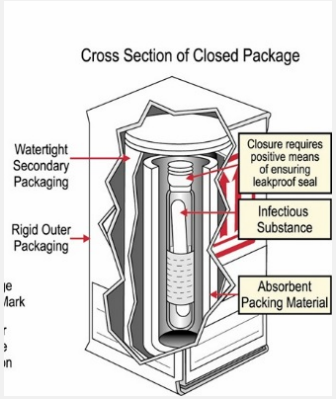


# STRIVE Laboratory Testing

- Second aliquot of blood in EDTA collected from possible case
- Triple packed and transported at 2-10°C to CDC laboratory in Bo
- Specimen aliquoted for immediate testing and long-term storage
- Testing aliquot inactivated and RNA extracted
- RNA tested by reverse transcriptase real-time PCR for two Ebola virus targets (NP and VP40) and human RNaseP as described
- Assays performed as specified under FDA Emergency Use Authorization and guided by Good Clinical Laboratory Practice standards
- Chain of custody documented

# STRIVE Laboratory Testing

- Second aliquot of blood in EDTA collected from possible case (separate from diagnostic workflow)

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